Biofilm Claims for Disinfectant Products

EPA's Regulatory Perspective

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Goals of this Presentation

- Discuss EPA's role in the regulation of disinfectant products (i.e., antimicrobial pesticides) and how this is related to potential products designed to treat inanimate surfaces contaminated with biofilm.
- An update will be provided on product performance methods and initial considerations for EPA's regulatory guidance.

Topic Areas for Discussion

- OPP Microbiology Laboratory
- Disinfectant Product Registration
- Test Methods of Interest – the ASTM Single Tube Method
- Draft EPA Guidance/Potential Claims
- Next Steps

EPA's Office of Pesticide Programs (OPP) Microbiology Laboratory Branch (MLB)

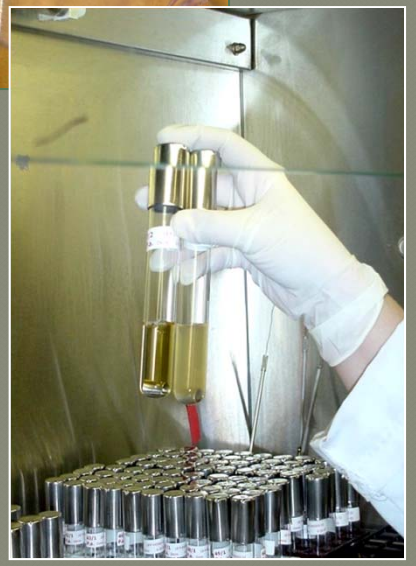
- Located at the Environmental Science Center, Fort Meade, MD
- Expertise in testing the efficacy of EPA-registered disinfectants
  - Wide range of formulations
  - Products are tested against clinical pathogens
- Conduct the Antimicrobial Testing Program – a surveillance initiative
- Lead research and development on new test methods
- Lead collaborative studies to improve and develop standard methodologies
- Work with standard setting organizations on method related issues
- Work with stakeholders on method use and standardization

Disinfectant Product Registration

- Under Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), EPA is responsible for the registration of pesticidal products
- Disinfectants (antimicrobial pesticides) are substances used to destroy or suppress the growth of harmful microorganisms such as bacteria, viruses, or fungi on inanimate environmental surfaces.
- Disinfectants bearing label claims for control of microorganisms on inanimate environmental surfaces which are infectious to man are considered directly related to human health – these are known as **public health disinfectants**.
- Under FIFRA, the registrant of a disinfectant product with a **public health claim** is required to submit **efficacy** data to EPA in support of the product's registration.

Disinfectant Product Registration

- Public health disinfectants are marketed in several formulations including liquids, sprays, and towelettes.
- Standard laboratory test methods are in place to accommodate each formulation type.
- Efficacy test guidelines have been established to inform the manufacturer which test methodology is appropriate to support a specific efficacy claim.
- The AOAC International (AOAC), a standard-setting organization, maintains and publishes many of the disinfectant test methods in the AOAC Official Methods of Analysis.



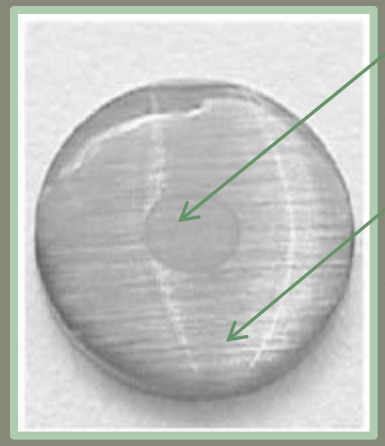
Disinfectant Product Registration

- The OPP Antimicrobials Division reviews the product efficacy data and if the requirements for registration are met, the product is granted a registration and is issued an EPA registration number.
- Currently, formal efficacy test guidelines have not been established by EPA to inform the registrant which test methodology and microorganisms are appropriate to support **biofilm** claims.
- However, an EPA interim guidance document has been drafted and the basic concepts will be discussed later in this talk.

Disinfectant Product Registration

- To meet the regulatory challenges involving novel products, claims, and the emergence of new clinical pathogens, the EPA is systematically developing and assessing new quantitative efficacy methods.
- Assessing the performance of a test method across multiple laboratories is desirable.
- Collaborative studies are used to assess the clarity and accuracy of test protocols, and to generate method performance indicators.

OECD Quantitative Method



Disinfectant Product Registration

- Biofilm is considered to be a “pest” by the EPA.
- Therefore, any disinfectant label claim to prevent, destroy, repel or mitigate biofilm on an inanimate environmental surface is a pesticidal claim which requires registration under FIFRA – including product efficacy data.
- Biofilm express unique characteristics, and therefore require unique and relevant test methods for measuring product efficacy.
- The choice of method will dictate the type of label claim.

Test Methods for Biofilm

- The EPA is considering the use of ASTM method E2871-12 (Evaluating Disinfectant Efficacy against *Pseudomonas aeruginosa* Biofilm using the Single Tube Method) as a regulatory method.
- This quantitative method was collaboratively developed by EPA and Montana State University (MSU) Center for Biofilm Engineering.
- MSU led a interlaboratory study (ASTM) in 2012/2013
- Biofilm is produced using the CDC biofilm reactor procedure (ASTM method E2562-12).
- To gain further experience with the Single Tube Method, EPA conducted a series of in-house efficacy tests on several registered disinfectants (without biofilm claims).

Test Methods for Biofilm

- EPA's study was used to develop an in-house Standard Operating Procedure (SOP MB-20) based on the ASTM standard and to support the development of EPA's Interim Guidance on biofilm claims.
- The resulting data, in conjunction with findings from a recently completed ASTM inter-laboratory study, will be used to inform the EPA on best practices for use, potential types of claims, and a performance standard.

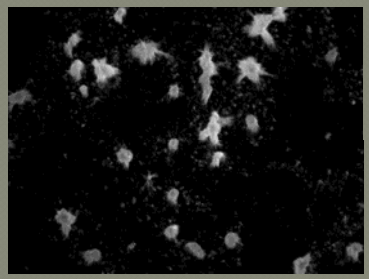
MLB Study Goals/Phases

- **Phase 1**: Generate control carrier counts for *P. aeruginosa* and *S. aureus*
  - Evaluate the level and consistency of control carrier counts
  - Currently, the ASTM methods only address growth of *P. aeruginosa* biofilm, thus modifications were made for growing of *S. aureus*
- **Phase 2**: Efficacy evaluation of disinfectants against *P. aeruginosa* and *S. aureus*
  - Determine the efficacy of commercially available disinfectants
  - 6 ready-to-use products and 2 concentrated products
  - The products were evaluated with a 10 minute contact time using the label concentration

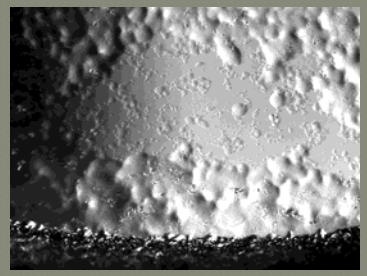
Test Methods for Biofilm
CDC Biofilm Reactor

Eight Rods per reactor

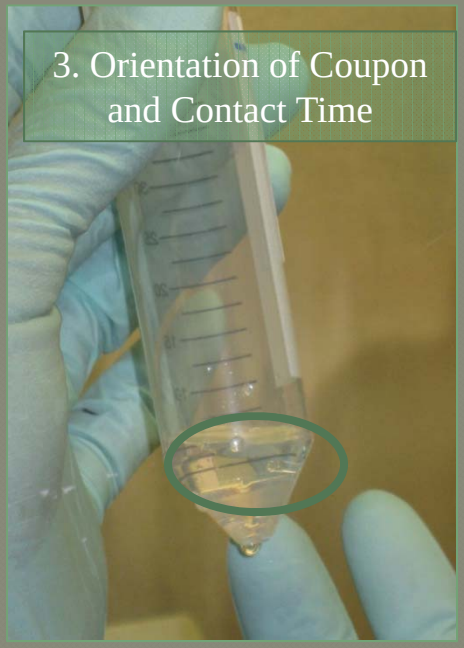
Three coupons per rod

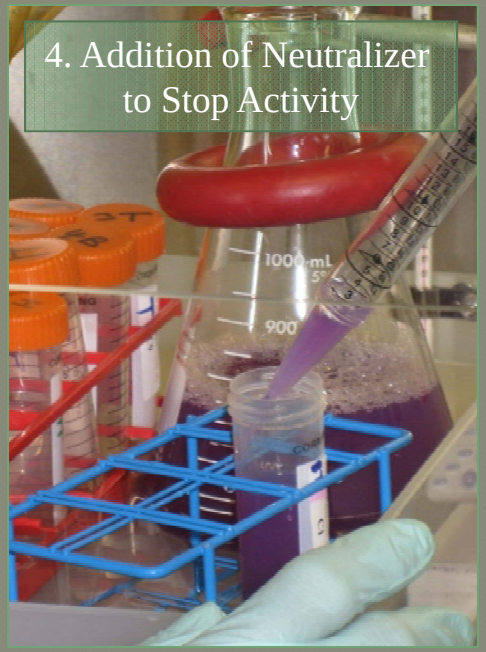


Multiple carrier materials available

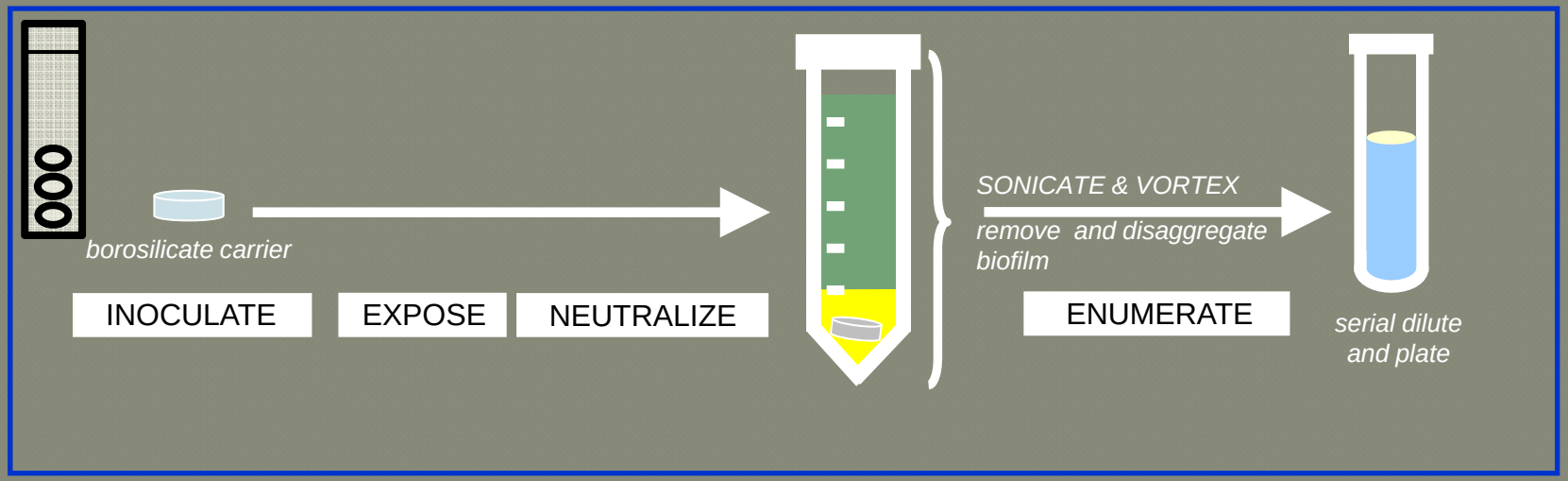


Test Methods for Biofilm Single Tube Method





Single Tube Method
Basic principles

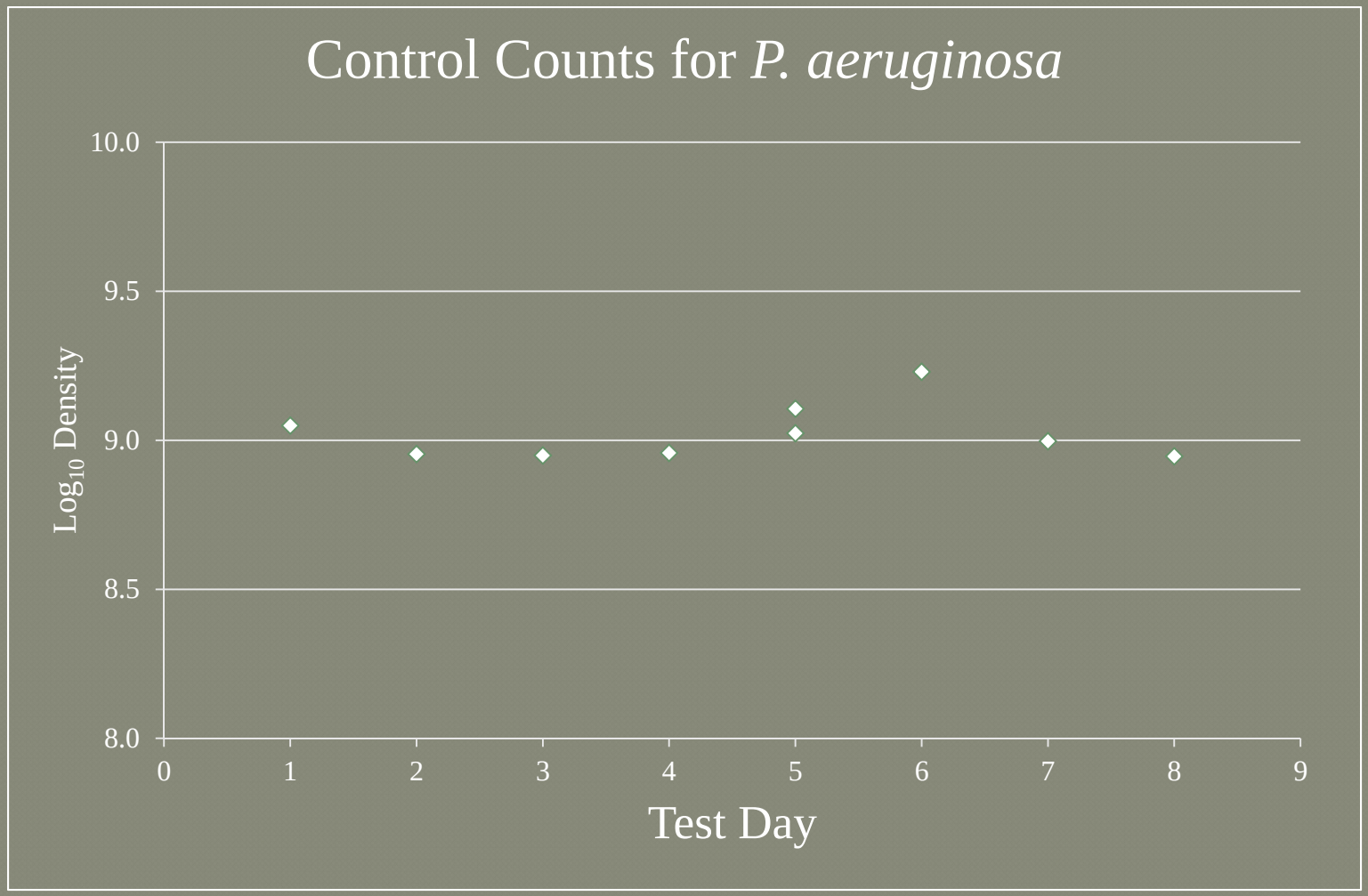


Key Aspects/Steps:

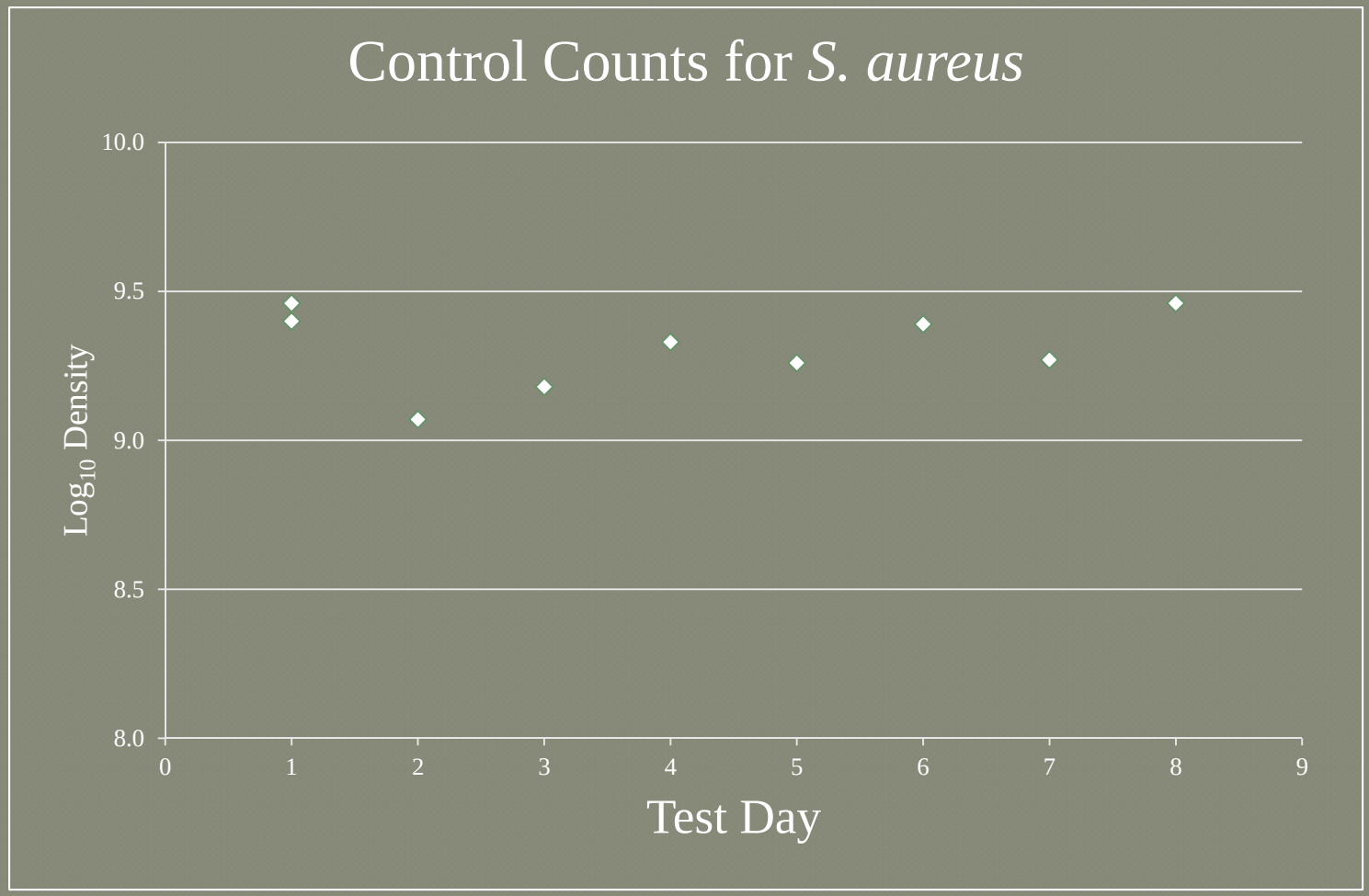
- 4 mL disinfectant
- 36 mL neutralizer
- Variable contact times & concentrations
- 20±1°C treatment temperature

- Vortex 30 s
- Sonicate 30 s
- Repeat twice
- Vortex 30 s

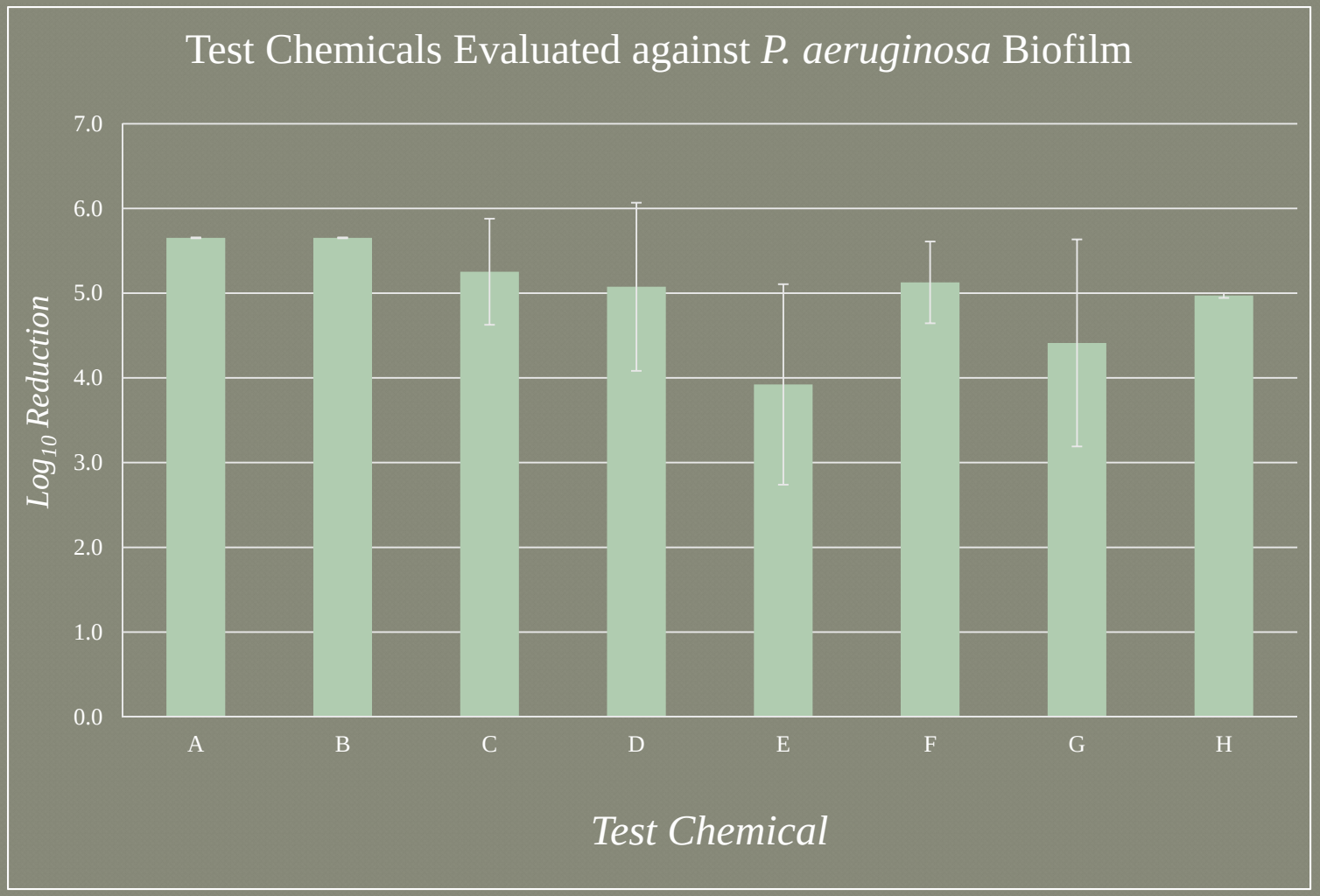
Single Tube Method Results



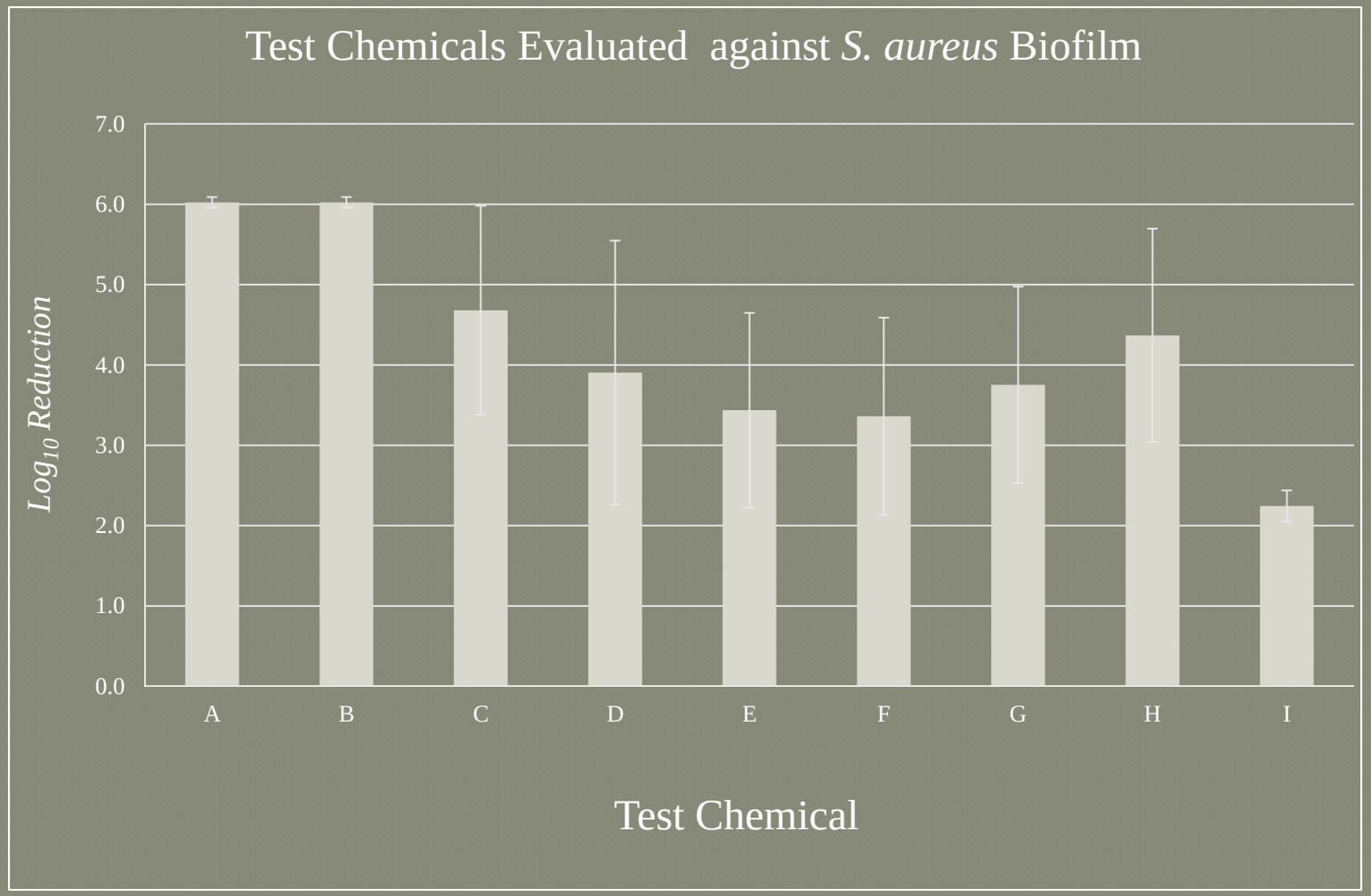
Single Tube Method Results



Single Tube Method Results



Single Tube Method Results



Single Tube Method
Attributes

- **Desirable:**
  - Closed system
  - Combined removal and disaggregation
  - Easier to perform
  - Use of conical vial allows for smaller volume of disinfectant
  - Decreased potential for technician bias
- **Limitations:**
  - Method does not distinguish between kill and removal
  - Concern about synergistic kill
  - Challenges associated with standardizing sonication parameters

Single Tube Method
General Observations

- The Single Tube Method was found to be easy-to-follow and capable of evaluating basic biofilm claims related to a reduction in bacteria in biofilm.
- Control counts for both microbes were consistent over test days
- Several disinfectants exhibited log reduction levels at 5 or above.
  - These are conservative estimates due to the dilutions plated and substitution values (for counts of zero)
  - Variability was observed between the treated coupons – more for *S. aureus*

Draft Guidance for a Biofilm Claim

- Basic Strategy Under Consideration
  - Use ASTM E2871-12 (Single Tube Method)
  - A claim for controlling biofilm may be added to a registered disinfectant product with an existing antimicrobial claim.
  - Borosilicate glass coupons
  - Evaluate three batches of product at the lower certified limit (LCL).
  - Evaluate a minimum of five carriers against the disinfectant and 3 carriers as controls.
  - Conduct neutralization testing in advance of efficacy testing to determine the appropriate neutralizer for the product.
  - A minimum 5 log reduction in viable bacteria in biofilm is required.

Biofilm Claims Under Consideration

- Kills 99.999% of bacteria in biofilm on a hard, non-porous surface
- Kills a minimum of 99.999% of bacteria in biofilm
- Reduces at least 99.999% of bacteria growing in biofilm
- Other related claims:
  - Kills biofilm bacteria
  - Controls slime-forming bacteria
  - Specifically designed and formulated to destroy bacteria in biofilm
  - Penetrates biofilm, killing the bacteria living there
- Examples of site-specific claims
  - Household/residential settings
  - Healthcare settings
  - Industrial or food processing settings

Next Steps

- Propose revisions to the ASTM methods; especially for testing of *S. aureus* biofilm
- To increase accuracy of the assay
  - Filter the contents of reaction tube containing the carrier
- Pre-screening test chemicals may be necessary to determine the appropriate dilutions required to achieve countable plates
- Work with MSU on method performance criteria
- Incorporate our knowledge of the test methods and analysis of the data into an EPA guidance document

Acknowledgements

- EPA Data Generation
  - Rebecca Pines – EPA Microbiology Laboratory
  - Lisa Smith – Edgewood Chemical Biological Center

Useful Information

- EPA test method guidelines
  - http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series810.htm
- List of EPA registered disinfectants
  - http://www.epa.gov/oppad001/chemregindex.htm
- MLB Standard Operating Procedures:
  - http://www.epa.gov/pesticides/methods/atmpa2z.htm
- Published summary of efficacy test methods:
  - Tomasino, S.F. 2013. Development and assessment of disinfectant efficacy test methods for regulatory purposes. American Journal of Infection Control. 41, 572-576.